

precipitation at concentration factors above 20-25 fold (for 1 g/l ~~Pluronic~~ PLURONIC F-68 nonionic block copolymer in the media).

line 19 ke 1-18-10

In the specification at page 12, line 18, please replace Examples 2 and 3 with the following amended Examples 2 and 3:

#### Example 2

##### Co-Concentration of ~~Pluronic~~ PLURONIC F-68 Nonionic Block Copolymer

The average molecular weight of ~~Pluronic~~ PLURONIC F-68 nonionic block copolymer is 8.4 kD, which is relatively large. Due to the formation of secondary membranes during ultrafiltration processes and the inherently inhomogeneous conditions along the crossflow channel, the selectivity of conventional UF technology does usually not allow significant separation of molecules in the size range of ~~Pluronic~~ PLURONIC nonionic block copolymer. Even for 100 kD UF membranes, as used for the largest protein products like rFVIII or gp220/350, significant retention and co-concentration of polymers like ~~Pluronic~~ PLURONIC F-68 nonionic block copolymer is usually found (see e.g. Schulz et al., 1997). It can be assumed that the retention coefficient R of ~~Pluronic~~ PLURONIC F-68 nonionic block copolymer during the ultrafiltration process with, e.g., a 10 kD NMWCO (nominal molecular weight cut-off) will be close to 1 (or 100%). Since the ~~Pluronic~~ PLURONIC F-68 nonionic block copolymer concentration in the medium required to obtain adequate cell protection during fermentation is 1 g/l (0.1%), 30 fold concentration would therefore lead to up to 30 g/l (or 3%) ~~Pluronic~~ PLURONIC F-68 nonionic block copolymer in the UF concentrate.

To confirm this hypothesis, retentate samples of various concentration factors (1X = culture supernatant, 2X, 4X, 8X, 16X and approx. 50X) were submitted for analysis by Thin Layer Chromatography (TLC). The resulting ~~Pluronic~~ PLURONIC F-68 nonionic block copolymer concentrations were estimated as 1-2 g/l for 1 and 2X, 4 g/l for 4X, 4-10 g/l for 8X, 10 g/l for 16X and 50 g/l for 50X. Considering the inherent inaccuracy of the TLC method, these